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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/837,217	04/19/2001	Chia Ning (Sophia) Chang		6921

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DEPARTMENT OF PLASTIC SURGERY
5 FU-HSING STREET
KWEI-SHAN, TAO-YUAN, 333
TAIWAN

EXAMINER	
NGUYEN, QUANG	
ART UNIT	**PAPER NUMBER**
1633	

MAIL DATE	DELIVERY MODE
11/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/837,217	CHANG, CHIA NING (SOPHIA)	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-6 and 11-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-6 and 11-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/11/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on 12/14/06 was entered.

Amended claims 1-2, 4-6 and 11-14 are pending in the present application, and they are examined on the merits herein.

Response to Amendment

The rejection under 35 U.S.C. 112, first paragraph, was withdrawn in light of Applicant's amendment.

The rejection under 35 U.S.C. 102(b) as being anticipated by Moutsatsos et al. (WO 99/11664) was withdrawn in light of Applicant's amendment.

The rejection under 35 U.S.C. 102(b) as being anticipated by Riew et al. (Calcif. Tissue Int. 63:357-360, 1998) as evidenced by Caplan et al. (U.S. 5,855,619) was withdrawn in light of Applicant's amendment.

The rejection under 35 U.S.C. 102(a) as being anticipated by Cheng et al. (Calcif. Tissue Int. 68:87-94, 2001) as evidenced by Caplan et al. (U.S. Patent No. 5,855,619) was withdrawn in light of Applicant's amendment.

The rejections under 35 U.S.C. 103(a) based upon Moutsatsos et al. (WO99/11664; Cited previously) and Kadiyala et al. (US 6,541,024) were withdrawn in light of Applicant's amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Amended claims 1-2, 5-6 and 11-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moutsatsos et al. (WO99/11664; Cited previously) in view of Kadiyala et al. (US 6,541,024) and Vacanti et al. (US 6,171,610). ***This is a new ground of rejection.***

Moutsatsos et al. disclose the preparation of bone marrow stromal cells transformed with a recombinant replication-deficient adenovirus vector (e.g., E1 deleted; E1, E3, E4 deleted recombinant adenoviruses) expressing one or more bone morphogenetic proteins that include human BMP-2 for regeneration of bone formation *in vivo* (see Summary of the invention and at least example 14, pages 41-50). Moutsatsos et al. also teach that the recombinant cells can be administered in combination with an appropriate matrix for supporting the composition, and this matrix can be in the form of biocompatible matrix biomaterials (a pharmaceutically acceptable polymer) including polylactic acid, polyanhydrides, calcium sulfate, bone, dermal collagen, hydroxyappatite, aluminates, pure proteins or extracellular matrix components and others (line 32 on page 6 continues to line 27 on page 7). Furthermore, Moutsatsos et al. teach that their delivery system for rhBMP-2 can be applied locally or regionally (see examples 13-14; particularly page 41, lines 15-17 and line 34 of page 45 continues to line 2 of page 46).

Moutsatsos et al do not teach specifically a method for enhancing bone formation in a subject comprising a step of applying a biodegradable plate to a site requiring new bone formation, and/or the genetically modified bone marrow stromal cells expressing heterologous BMP-2 protein are present in a concentration of about 50 x 10^6 per ml of polymer.

However, at the effective filing date of the present application Kadiyala et al already taught a method for augmenting bone formation using isolated mesenchymal stem cells with a ceramic material or matrix in the presence of fixation devices such as polyethylene fixation plate (a biodegradable plate) or a SynthesR 8-hole lengthening plate which are internally placed and secured (see abstract; col. 4, lines 45-47; col. 11, lines 24-29; col. 20, lines 2-4; col. 22, lines 40-45).

Moreover, Vacanti et al also taught a method of generating new tissue in a patient, including new bone, by delivering a liquid hydrogel-cell composition, which contains a hydrogel and tissue precursor cells, into a permeable, biocompatible support structure, wherein the hydrogel can support very large density of cells such as but not limited to 50 million cells/ml (see at least Summary of the Invention). Examples of different hydrogels include polysaccharides such as alginate, polyphosphazenes and polyacrylates (col. 9, lines 24-53), and examples of support structures include porous polymer meshes, natural and synthetic sponges made of a biocaompatible or biodegradable, synthetic polymer such as a polyglycolic acid containing polylactic acids that bond the polyglycolic fibers, and others (col. 6, line 31 continues to line 64 of col. 7).

Accordingly, it would have been obvious for an ordinary skill artisan to modify the method taught by Moutsatsos et al. by also applying a biodegradable fixation plate or a biodegradable/biocompatible structure support at a site requiring new bone formation in a subject and/or use the genetically modified bone marrow stromal cells expressing heterologous BMP-2 at a concentration of 50 million cells/ml of a hydrogel polymer such as aginate in light of the teachings of Kadiyala et al and Vacanti et al. as discussed above.

An ordinary skilled artisan would have been motivated to make the above modifications because the use of a biodegradable fixation plate and/or a biodegradable/biocompatible structure support at an injured bone area or a site requiring new bone formation is routinely used in a bone repair operation as taught at least by Kadiyala et al. and Vacanti et al. Furthermore, an ordinary skilled artisan would have been motivated to use a composition comprising a liquid hydrogel-tissue precursor cells (e.g., the genetically modified bone marrow stromal cells) at a concentration of 50 million cells/ml because Vacanti et al already taught that hydrogel can support very large densities of cells and that hydrogel allows diffusion of nutrients and waste products to, and away from, the cells, which promotes tissue growth (see at least col. 1, line 58 continues to line 2 of col. 2).

An ordinary skilled artisan would have a reasonable expectation of success to carry out the above modification in light of the teachings of Moutsatsos et al., Kadiyala et al, and Vacanti et al., coupled with a high level of skills of an ordinary skilled artisan in the relevant art.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Amended claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Moutsatsos et al. (WO99/11664) in view of Kadiyala et al. (US 6,541,024) and Vacanti et al. (US 6,171,610) as applied to claims 1-2, 5-6 and 11-14 above, and further in view of Riew et al. (Calcif. Tissue Int. 63:354-360, 1998). ***This is a new ground of rejection.***

The teachings of Moutsatsos et al., Kadiyala et al. and Vacanti et al. have been discussed above. However, none of the references teaches specifically the use of collagen type I as a pharmaceutically acceptable polymer.

However at the filing date of the present application Riew et al already taught the preparation and transduction of bone marrow mesenchymal stem cells isolated from bone marrow cells with a recombinant adenoviral vector expressing human BMP-2 for transplantation in a rabbit spinal fusion model in the form of a suspension of a type I collagen solution, Pancogene S (see at least Materials and Methods on page 358; and Figures 2-4).

Accordingly, it would have been obvious for an ordinary skill artisan to further modify the method of Moutsatsos et al., Kadiyala et al and Vacanti et al. by also using Pancogene S as a pharmaceutically acceptable polymer or as a hydrogel in light of the teachings of Riew et al.

An ordinary skilled artisan would have been motivated to make the above modification because Riew et al already successfully used Pancogene S as a pharmaceutically acceptable carrier to deliver genetically modified mesenchymal stem cells expressing human BMP-2 to induce bone formation in a rabbit spinal fusion model.

An ordinary skilled artisan would have a reasonable expectation of success to carry out the above modification in light of the teachings of Moutsatsos et al., Kadiyala et al., Vacanti et al., and Riew et al., coupled with a high level of skills of an ordinary skilled artisan in the relevant art.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Conclusions

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's SPE, Joseph T. Woitach, Ph.D., may be reached at (571) 272-0739.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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QUANG NGUYEN, PH.D.
PRIMARY EXAMINER